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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/707,087	11/06/2000	Carl H. June	RPI-034CPCN	8859

959 7590 11/17/2004

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/707,087	JUNE ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 32-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 32-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 8/24/04 have been entered. No claims have been amended. Claims 1, and 32-46 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 32-46 stand rejected under 35 U.S.C. 112, second paragraph, for reasons of record and in view of applicant's response to the previous Office action.

With respect to the assumption of the Office, "For the sake of a compact prosecution, the dosing range of 0.1 to 10 μg/ml would be used as the standard for the submitogenic amount", which is concluded based on the teaching of *June et al*, and the specification, wherein only a specific dose was taught (1 μg/ml), applicants argue that June et al teach that the optimal concentration must be determined experimentally, and although the dose for T cells to proliferate overlaps with the dose that is submitogenic, applicants submit that one skilled in the art recognizes that with each and every antibody, each type of cell, and each culture system, the exact dosage of the antibody will vary and must determined experimentally.

In response, it is true that for each antibody and each type of cell, the submitogenic dose may be different; but remember the claims are limited to anti-CD3, and T cell. And June et al clearly teach, ""WITH OKT3, THE OPTIMAL CONCENTRATION WAS **DETERMINED** TO BE TYPICALLY IN THE RANGE OF 0.1 TO 10 MICROGRAMS PER MILLILITER" (emphasis added). If applicants insist that this dosing range is not submitogenic for T cells, then, why applicants used it and call it submitogenic? Since the mitogenic (0.1-10 μg/ml) and submitogenic (1 μg/ml) doses are overlapping, the specification fails to teach how to distinguish the submitogenic amount from the mitogenic amount? And what is the submitogenic dose of the anti-CD3 antibody for T cells. Thus, the metes and bounds of the claims are unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 32-46 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and following.

Before getting into details of the arguments, let us not forget that the following disputed art of record were initially cited by the Office for the purpose of pointing out the discrepancy and unpredictability of the state of the art with respect to the effect of anti-CD3 and anti-CD28 on T cells.

In 8/24/04 response, applicants again argue that Kwon et al use high dose of anti-CD3 antibody, not a submitogenic amount, and repeated activation.

In response, it has been indicated previously and reiterated here that *Kwon et al* do use mature peripheral T cells (PBMC, column 20, lines 53-55), for contacting of anti-CD3 at an amount exactly like the specification, i.e. 1 μg/ml soluble anti-CD3 mAb (column 17, line 31), and the instant claims are not limited to a single dose activation. Accordingly, the arguments are not persuasive.

Applicants then argue that claim recitation of *mature* in the pending claims excludes Jurkat cells. In response, if so, this introduces new matter to the disclosure, since this exclusion was not in the original disclosure. Assuming *arguendo* the subject matter was disclosed in the original specification, such exclusion should be reflected in the claim. This is because as noted in MPEP § 2111, claims must, under modern claim practice, stand alone to define invention. It is not proper to read limitations appearing in the specification into the claim when these limitations are not recited in the claim. See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671 (Fed. Cir. 1994); *Intervet America Inc. v Kee-Vet Lab. Inc.*, 887 F.2d 1050, 1053, 12 USP2d 1474, 1476 (Fed. Cir. 1989). Words of the claim are generally given their ordinary and customary meaning, unless it appears from the written description that they were used differently by the applicant. Since the specification does not redefine the word "mature", and the claims do not exclude Jurkat cells, the argument is not persuasive.

Applicants then argue that *Lenardo* teach the effect of IL-2 will wear off 2-3 days after IL-2 exposure. In response, it is noted *Lenardo* teaches, "A CRITICAL DETERMINANT OF

THE CHOICE BETWEEN T LYMPHOCYTE PROLIFERATION OR PROGRAMMED CELL DEATH IS THE PRIOR EXPOSURE OF THESE CELLS TO IL-2" (column 1, lines 48-64), there is no teaching regarding the time limitation after IL-2 exposure. In view of such teaching, the claims do not seem to be enabled for T cells previously exposed to IL-2.

With respect to the superantigens, Applicants argue that cited references are highly speculative and are not supported by experimental evidence. Applicants cited long paragraph highlighting that Johnson et al used the words, "preliminary evidence", "may", and "possibly". In response, it is noted that preliminary evidence is experimental evidence. And it is also noted that there is no experimental evidence provided by the specification for the contemplated agents beyond anti-CD3 and anti-CD28, not even a preliminary one. Applicants are reminded that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the prior art products do not necessarily or inherently possess characteristics of claimed product, which requires factual evidence demonstrating that actual, unobvious differences exist or the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989). Applicants further pointed to example 7 of the specification for support. It is noted though the example is drawn to expressing bcl-xl protein in cultured

cells, and has nothing to do with *superantigens*. The specification fails to provide any evidence that any of the superantigens, lectins, and calcium ionophore molecules would increase intracellular bcl-Xl.

Applicants then argue that both Lenardo et al and Lynch et al teach a phenomenon that occurred in vivo, whereas the claimed method is ex vivo. In response, claim 39 and dependent claims are drawn to an *in vivo* method.

It is noted that Applicants argued on one hand that both Lenardo et al and Lynch et al teach a phenomena that occurred in vivo, and argued on the other hand that the examiner has failed to provide teachings in the art that indicate the claimed methods would not work. In response, all of the cited references are evidence illustrating the state of the art and unpredictability in the art, which references range from *in vitro* studies to *in vivo* studies. Since the cited references illustrated the unpredictability of the relevant art, and certain contradictions in the teaching of the specification, and since the claimed method is supposed to be novel, i.e. lacking of art of record, it is incumbent upon applicants to provide sufficient teaching to guide the practice of the invention. For example, the unpredictability lies on the complexity of the TcR/CD3 complex. *Wolf et al* (Eur J. Immunol 1994;24:1410-7) teaches that anti-CD3 antibody "TURNED OUT TO EXERT SEEMINGLY OPPOSING EFFECTS ON T CELL FUNCTION DEPENDING ON THE DIFFERENTIATION STATE AND EXPERIMENTAL CONDITIONS" (1st paragraph, page 1410). On top of all these, T cells function in different subtypes in vivo, once the resting T cells activated, they may be helper, suppressor, cytotoxic, and memory etc., each subtype responds to particular activators such as an antigen or a cytokine. The art of record is silent and the

specification fails to teach the circumstance necessary to introduce these generalized mature T cells into a subject, or once they are activated, or differentiated, whether the *ex vivo* observed protective effect would remain; the specification fails to teach how to deal with the differentiation state, experimental conditions, and even more complicated *in vivo* conditions affecting T cell function as taught by *Wolf et al*, thus, the specification fails to provide an enabling disclosure to guide the practice of the invention. MPEP requires that the specification must teach those of skill in the art how to practice the invention, not to figure out for themselves. To this end, the principle is "IF LITTLE IS KNOWN IN THE PRIOR ART ABOUT THE NATURE OF THE INVENTION AND THE ART IS UNPREDICTABLE, THE SPECIFICATION WOULD NEED MORE DETAIL AS TO HOW TO MAKE AND USE THE INVENTION IN ORDER TO BE ENABLING. THE "PREDICTABILITY OR LACK THEREOF" IN THE ART REFERS TO THE ABILITY OF ONE SKILLED IN THE ART TO EXTRAPOLATE THE DISCLOSED OR KNOWN RESULTS TO THE CLAIMED INVENTION. IF ONE SKILLED IN THE ART CAN READILY ANTICIPATE THE EFFECT OF A CHANGE WITHIN THE SUBJECT MATTER TO WHICH THE CLAIMED INVENTION PERTAINS, THEN THERE IS PREDICTABILITY IN THE ART. ON THE OTHER HAND, IF ONE SKILLED IN THE ART CANNOT READILY ANTICIPATE THE EFFECT OF A CHANGE WITHIN THE SUBJECT MATTER TO WHICH THAT CLAIMED INVENTION PERTAINS, THEN THERE IS LACK OF PREDICTABILITY IN THE ART. ACCORDINGLY, WHAT IS KNOWN IN THE ART PROVIDES EVIDENCE AS TO THE QUESTION OF PREDICTABILITY. IN PARTICULAR, THE COURT IN IN RE MARZOCCHI, 439 F.2D 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), STATED: [I]N THE FIELD OF CHEMISTRY GENERALLY, THERE MAY BE TIMES WHEN THE WELL-KNOWN UNPREDICTABILITY OF CHEMICAL REACTIONS WILL ALONE BE ENOUGH TO CREATE A REASONABLE DOUBT AS TO THE ACCURACY OF A PARTICULAR BROAD STATEMENT PUT FORWARD AS ENABLING SUPPORT FOR A CLAIM. THIS WILL ESPECIALLY BE THE CASE WHERE THE STATEMENT IS, ON ITS FACE, CONTRARY TO GENERALLY ACCEPTED SCIENTIFIC PRINCIPLES. MOST OFTEN, ADDITIONAL FACTORS, SUCH AS THE

TEACHINGS IN PERTINENT REFERENCES, WILL BE AVAILABLE TO SUBSTANTIATE ANY DOUBTS THAT THE ASSERTED SCOPE OF OBJECTIVE ENABLEMENT IS IN FACT COMMENSURATE WITH THE SCOPE OF PROTECTION SOUGHT AND TO SUPPORT ANY DEMANDS BASED THEREON FOR PROOF. [FOOTNOTE OMITTED.] (MPEP 2164.02, 03). The Office relied on the combined teachings of the prior- and post-filing date art to provide a reasonable basis to show that one skill in the art could not practice the invention without undue experimentation. "WHEN CONSIDERING THE FACTORS RELATING TO A DETERMINATION OF NON-ENABLEMENT, IF ALL THE OTHER FACTORS POINT TOWARD ENABLEMENT, THEN THE ABSENCE OF WORKING EXAMPLES WILL NOT BY ITSELF RENDER THE INVENTION NON-ENABLED." "LACK OF A WORKING EXAMPLE, HOWEVER, IS A FACTOR TO BE CONSIDERED, ESPECIALLY IN A CASE INVOLVING AN UNPREDICTABLE AND UNDEVELOPED ART." (MPEP 2164.02, 03) Otherwise, according to the logistics of the applicants, some of the cited art of record would have reasonably anticipated instantly claimed invention. Since the specification provides **no** evidence with respect to how the treated T cells would behave in vivo, the functionality and pharmacokinetics of these T cells, and conditions for using such cells, and overall effects on T cells in vivo, it fails to provide enablement for what is now claimed. The Federal Circuit has stated that:

> a specification need not disclose what is well known in the art. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, **when there is no disclosure** of any specific starting material **or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art**. It is the specification, not the knowledge of one skilled in the art, that must

> supply the novel aspects of an invention in order to constitute adequate enablement.

Genentech Inc. v. Novo Nordisk A/S, 42 USPQ2d 1005 (CAFC 1997) (emphasis added).

With respect to the combination of agents, Applicants argue that it is true that figure 5 shows that CD28 alone did not induce detectable amounts of BCL-XL, but the pending claims require the combination of at least 2 agents. In response, the claims encompass any combination of two recited agents including the combination of CD28 and lectin without the presence of anti-CD3. However, the specification and the numerous cited art of record (see sections following) have shown that the presence of, or pre-exposure to the anti-CD3 antibody appeared to be a pre-requisite for increased levels of BCL-Xl such as those shown in figure 2 and experiment 2. The specification fails to provide any evidence that in the absence of the anti-CD3, any other combination would result in T cell protection. There is no evidence what so ever that a divalent calcium ionophore ionomycin combined with a lectin would lead to increased intracellular expression of Bcl-X. Thus, the specification fails to support the full scope of the invention.

Accordingly, for reasons of record and set forth *supra*, the specification fails to meet the statutory enablement requirement.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

(f) he did not himself invent the subject matter sought to be patented.

Claims 1, 32-35, 37, and 38 stand rejected under 35 U.S.C. 102(e) as being anticipated by *June et al* (US 6,352,694, and 6,534,055).

In 8/24/04 response, applicants argue that the pending claims require the dose of anti-CD3 to be submitogenic, whereas the anti-CD3 utilized by June et al causes cells to proliferate, thus not submitogenic. Applicants go on to argue that June et al do not provide any teaching that a T cell treated with the claimed agents would increase Bcl-Xl protein levels.

The arguments have been fully considered, but they are not persuasive for reasons of record and following.

The claimed method and the cited art utilize the same starting materials and method steps, i.e. contacting T cells *in vitro* with an anti-CD3 antibody, and an anti-CD28 antibody or an anti-CD2 antibody, or PHA, wherein the dosing of the anti-CD3 antibody is within the dosing range of "submitogenic" as implied in the instant specification, thus, it would inherently achieve what it is claimed now. Accordingly, the cited patents anticipate the instant claims.

Applicants is again reminded that claim recitation "for protecting a mature T cell from cell death" have not been given patentable weight in this rejection because they

merely recite an intended use of the process. Please note that intended use limitations bear little weight on the determination of novelty of the invention. This is because a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

It is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff* 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990); *In re Swinehart*, 439 F. 2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993). MPEP 2112.01 states that "PRODUCTS OF IDENTICAL CHEMICAL COMPOSITION CAN NOT HAVE MUTUALLY EXCLUSIVE PROPERTIES.' A CHEMICAL COMPOSITION AND ITS PROPERTIES ARE INSEPARABLE". THEREFORE, IF THE PRIOR ART TEACHES THE IDENTICAL CHEMICAL STRUCTURE, THE PROPERTIES APPLICANT DISCLOSES AND/OR CLAIMS ARE NECESSARILY PRESENT. *IN RE* SPADA, 911 F.2D 705, 15 USPQ2D 1655, 1658 (FED. CIR. 1990).

Applicants are reminded that the analysis set forth *supra* also applies to the following rejections, and will not be reiterated.

Claims 1, 35, 36, 37, and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Groux et al* (J Exp Med 1992;175:331-340).

Applicants argue that in the cited art a proliferative amount of anti-CD3 was required, thus the anti-CD3 is mitogenic amount, not submitogenic.

In response, the claimed method and the cited art utilize the same starting materials and method steps, i.e. contacting matured human T cells *in vitro* with an anti-CD3 antibody, plus anti-CD28, PHA, PWA, and superantigen SEB, wherein the dosing of the anti-CD3 antibody is within the dosing range of "submitogenic" as implied in the instant specification, thus, it would achieve what it is now claimed. Moreover, *Groux et al* clearly teach that anti-CD28 prevented T cell apoptosis (protecting a mature T cells from cell death, e.g. abstract). Accordingly, *Groux et al* anticipate instant claims.

Claims 1, 32, and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Wolf et al* (Eur J Immunol 1994;24:1410-17).

Applicants argue that Wolf et al teach using a mitogenic concentration of anti-CD3. In response, *Wolf et al* used the amount of anti-CD3 ranges from 0.01-10 μg/ml including the amount used in the specification, i.e. 1 μg/ml, thus the cited art meets the requirement for submitogenic amount, and claim limitation.

Claims 1, 32 and 38 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Lederman et al* (US 6,610,294).

Applicants argue that Lederman et al teach inhibiting autoimmune disease, not protecting mature T cells. Applicants is again reminded that intended use limitations bear little weight on the determination of novelty of the invention. Since the processes of

the cited patent and instant claims both comprising the steps of contacting the T cell with two agents selected from the group consisting of anti-CD3 antibody, anti-CD28 antibody, a CD28 ligand, and IL-2, thus, the two processes are indistinguishable.

Claims 1, 32-35, 37, and 38 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Gary et al* (US 5,883,223).

Applicants argue that *Gary et al* teach inhibiting T cell activation of B cells. Applicants is again reminded that intended use limitations bear little weight on the determination of novelty of the invention. Since the processes of the cited patent and instant claims both comprising the steps of contacting the T cell with two agents selected from the group consisting of anti-CD3 antibody, anti-CD28 antibody, a CD28 ligand, and IL-2, thus, the two processes are indistinguishable.

Claims 1, 32-38 stand rejected under 35 U.S.C. 102(e) as being anticipated by *Thompson et al* (US 6,685,941).

Applicants argue that *Thompson et al* teach inhibiting T cell activation of B cells. Applicants is again reminded that intended use limitations bear little weight on the determination of novelty of the invention. Since the processes of the cited patent and instant claims both comprising the steps of contacting the T cell with two agents selected from the group consisting of anti-CD3 antibody, anti-CD28 antibody, a CD28 ligand, and IL-2, thus, the two processes are indistinguishable.

Claims 1, and 32-38 stand rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter, for reasons of record and set forth *supra*.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 32-35, 37, and 38 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 15-19, 31, and 32 of U.S. Patent No. 6,352,694.

Applicants reiterated the arguments as stated under § 102 (e), which have been addressed above, and will not be reiterate here.

Claims 1, 32-35, and 38 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,534,055.

Applicants argue that protection from apoptosis is not necessarily coincident with induction of cell proliferation, and they are two different processes. Applicants have identified a function of anti-CD3 in T cells which is independent of its proliferative activity.

In response, the cited art of record acknowledge different effects of anti-CD3 such as cited in *Wolf et al* (Eur J. Immunol 1994;24:1410-7), that anti-CD3 antibody "TURNED OUT TO EXERT SEEMINGLY OPPOSING EFFECTS ON T CELL FUNCTION DEPENDING ON THE DIFFERENTIATION STATE AND EXPERIMENTAL CONDITIONS" (1st paragraph, page 1410). However, during the examination of a patent application, a method claim is evaluated by the method steps, since the processes of the cited patent and instant claims both comprising the steps of contacting the T cell with two agents selected from the group consisting of anti-CD3 antibody, anti-CD28 antibody, a CD28 ligand, and IL-2, thus, the two processes are indistinguishable. Intended use limitations bear little weight on the determination of novelty of the invention. It is a general rule that merely discovering and claiming a new benefit to an old process cannot render the process again patentable. *In re Woodruff* 919 F. 2d 1575, 1577-78, 16 USPQ2d 1934, 1936-37 (Fed. Cir. 1990); *In re Swinehart*, 439 F. 2d 210, 213, 169 USPQ 226, 229 (CCPA 1971); and *Ex Parte Novitski*, 26 USPQ2d 1389, 1391 (Bd. Pat. App. & Int. 1993).

Accordingly, the inventions as claimed are co-extensive.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

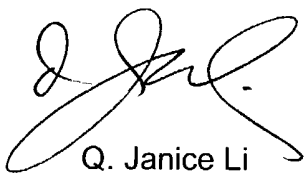
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Q. Janice Li
Primary Examiner
Art Unit 1632

GJL
November 12, 2004